REMARKS

Claims 1-15 are pending. Claims 1-15 stand rejected. Claims1, 6, and 7 have been amended. Support for the amended claims can be found in the specification and claims as originally filed.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Objections

Claims 1, 6 and 7 are objected to because of informalities. Claims 1 and 7 have been amended to address the Examiner's objection regarding claimed expressions. Claim 6 has been amended to provide proper antecedent basis. Applicants request the withdrawal of these objections.

35 U.S.C. § 112, first paragraph rejection

Claims 7-14 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Claim 7 has been amended to replace the phrase "prophylactically treating" to "inhibiting the onset or progression of" as suggested by the Examiner. Applicant requests the withdrawal of this rejection.

35 U.S.C. § 103(a) rejection

A. Powell in view of D'Amato, Kawai and Powell II

Claims 1, 4-6, and 15 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Powell et al. U.S. Patent No. 3,793,454 ("Powell") in view of D'Amato et al. U.S. Patent No. 5,712,291 ("D'Amato") and Kawai et al., Cancer Lett. 2001 Oct. 10; 171(2):201-07 ("Kawai"), and in further view of Powell et al., J. Pharmaceutical Sciences. August 1972 61(8):1227-1230 (hereinafter "Powell II").

Powell et al. discloses the use of herringtonine and isoherringtonine to treat L1210 and P388 leukemia tumors. Powell et al. fails to teach that each leukemia strain is an angiogenic disease and is not a solid tumor.

D'Amato asserts that angiogenesis is associated with blood-born tumors such as leukemias and that it plays a role in the abnormalities in the bone marrow that give rise to leukemic-like tumors.

Kawai et al. teaches that leukemic cell lines are representative of non-solid tumors.

As previously asserted by Applicant, Powell discloses the injection of tumor cells and the compound to be tested into the intraperitoneal cavity of test animals. In response, the Examiner has taken the position that (1) there is nothing in Powell to indicate that any specific protocol was followed regarding the implantation of L1210 or P388 cell lines in mice, and (2) the protocols disclosed in the In Vivo Cancer Model reference, previously submitted by Applicant, were published after the Powell filing date.

Enclosed herewith is the first part of a document entitled:"Protocols for Screening Chemical Agents And Natural Products Against Animal Tumors and Other Biological Systems" (3rd Ed.) May 24, 1972. As indicated in the Forward, this publication describes the antitumor screens of the National Cancer Institute ("NCI") that were first published in 1959 (Cancer Chemother Rep. 1:42-64 1959) and which appeared in greater detail in 1962 (Cancer Chemother Rep. 25:1-66 1962). (See column 1 of the Forward)

As compared to the earlier publication of this document in 1962, the number of test systems for which specific protocols are presented has been reduced from 24 to 6, which include the L1210 and P388 mouse leukemia systems (See Item 1 of the Forward.) Accordingly, the L1210 and P388 mouse leukemia systems were available prior to the filing date of Powell, i.e at least as early as 1962. As further indicated at Page 7 and 8 of the reference, the inoculation site for the L1210 and P388 leukemia cells for primary screening is the peritoneal cavity.

Accordingly, the skilled artisan would interpret Example 3 in Powell as calling for the implantation of leukemia L1210 or P388 cells into the peritoneal cavity. Further evidence of this can be found in Powell II which has the same named inventor and author. As indicated at page 1227, first paragraph, Powell II "showed activity against lymphoid leukemia L1210 and P388 leukemia in mice. The assays were performed as described in Cancer Chemother Rep., 25, 1 (1962). (See footnote 2, page 1227 and footnote "a" in Tables II and III.) This is the same

reference as cited in the reference submitted herewith which establishes the injection of the leukemia cells in the peritoneal cavity as of 1962.

Based upon the foregoing, Powell discloses the propagation of the L1210 and P388 cell lines in the mouse peritoneal cavity as an acites suspension followed by intraperitoneal injection of herringtonine and isoherringtonine. Such leukemia cell suspensions in the peritoneal cavity do not form solid tumors that require vascularization, as is know in the art. This being the case, the combined teachings of the cited art would not lead the skilled artisan to the conclusion that (1) the injection of herringtonine and isoherringtonine in the peritoneal cavity to treat suspended L1210 and P388 cells would result in an anti-angiogenic effect; and (2) that herringtonine and isoherringtonine would have any effect on a solid tumor that requires vascularization. It was the inventor, not the prior art, who discovered the anti-angiogenic property of cephalotaxines.

B. Chinery in view of D'Amato, Cecil's, O'Dwyer, and Medford

Claims 1-6 and 15 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chinery et al. U.S. Application No. 2001/0049349 ("Chinery") in view of D'Amato et al. U.S. Patent No. 5,712,291 ("D'Amato"), Cecil's Textbook of Medicine, pp. 1060-1074 ("Cecil's"), O'Dwyer et al., J. Clin. Oncol., 4:10(October), 1986, pp. 1563-1568 ("O'Dwyer") and Medford et al. U.S. Patent No. 5,380,747 ("Medford"), and in further view of Powell II. Applicants respectfully disagree.

Chinery is the primary reference and discloses the use of antineoplastic agents in combination with antioxidants to treat hyperproliferative conditions.

Claim 1 has been amended to state that the method for inhibiting angiogenesis consists essentially of contacting the host with a cephalotaxine. Since Chinery requires the combination with an antioxidant claim 1 as amended does not read on Chinery. This being the case, it is respectfully requested that the rejection be withdrawn.

Double Patenting Rejections

Claims 1-6 and 15 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 15-17 of copending Application No. 10/617,927. However, a Notice of Abandonment was issued on August 18, 2006. Applicants request the withdrawal of this rejection.

Claims 1-6 and 15 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over either of (i) Claims 1 and 16-21 of co-pending Application No. 67716-5002US1, or (ii) Claims 15-20 of co-pending Application No. 5003US02.

Claim 1 of co-pending Application No. 10/769, 638 claims a method of treatment of a host with a proliferative disease comprising contacting the host with homoharringtonine and camptothecin. As indicated, Claim 1 herein has been amended to indicate that the method consists essentially of contacting a host with a cephalotaxine. This being the case, the pending claims are patently distinct from those in the co-pending application.

Claim 15 of co-pending application No. 10/631, 106 is directed to a method of treating a host with a proliferative disease comprising contacting the host with amonafide in conjunction with homoharringtonine. Claim 1 as amended herein is patently distinct from Claim 15 in the co-pending application.

Based upon the foregoing, it is submitted that the double patenting rejections should be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1255.

Respectfully submitted,
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Dated: June 6 2007 By _____
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